Remarks/Arguments

The Claims

Claims 82-92 are currently pending in the application. Claim amendments have been introduced to further clarify the invention and do not introduce new matter and/or raise new issues requiring further consideration and/or search. Entry of the amendments is respectfully requested.

Rejection of Claims 82-92 under 35 U.S.C. 102(e)

Claims 82-92 are rejected as being anticipated by U.S. Patent No. 6,242,586 (hereafter the " '586 patent") to Gorman et al. The Examiner alleges that the '586 patent teaches antibodies to a mouse protein designated 499E9 which is said to be the same protein as mouse osteoprotegerin binding protein (hereafter "OPGbp") and which is said to be 84.1% identical to human OPGbp. It is further argued that the '586 patent teaches human monoclonal antibodies in view of the disclosure that monoclonal antibodies are to be prepared from human hosts (citing Example 5 and column 15, lines 65-67) and that antibodies may be modified to produce chimeric, humanized and recombinant forms (citing column 16, lines 10-33).

In order to anticipate the claimed invention, each element of the claimed invention must be found expressly or inherently in the '586 patent; and the '586 patent must enable one skilled in the art to practice the claimed invention without undue experimentation. See, for example, *Akzo N.V. v. United States ITC* 1 USPQ2d 1241 (Fed. Cir. 1986)). Applicant maintains that neither requirement for anticipation is met.

The '586 patent does not teach a human antibody that specifically binds to an OPGbp of SEQ ID NO:39. The patent does not disclose the sequence or structure of human OPGbp, so the Examiner relies upon the amino acid sequence homology of 84.1% between murine OPGbp and human OPGbp to argue that the claimed antibodies are anticipated by "cross-reacting" antibodies, antibodies that bind to both mouse and human OPGbp.

> However, given that the sequence of human and mouse osteoprotegerin binding proteins are substantially identical, it is reasonable that antibodies that specifically bind mouse osteoprotegerin binding protein as taught by Gorman et al. will also bind human osteoprotegerin binding protein. (Action at p. 4).

The Examiner has not provided any evidence or pointed to anything in the '586 patent disclosure to indicate that "cross reacting"antibodies which specifically bind mouse OPGbp would also specifically bind human OPGbp.

The '586 patent has not disclosed a method for preparing human antibodies which specifically bind human OPGbp. Example 5 allegedly discloses the preparation of antibodies specific for 499E9 by a method in which "synthetic peptides or purified protein are presented to an immune system to generate monoclonal and polyclonal antibodies" (col. 27, lines 66-67). However, one could not prepare antibodies specific for human OPGbp by this method since human OPGbp peptides or protein were not disclosed in the '586 patent. It is alleged that the disclosure at column 15, lines 66-67 and column 16, lines 10-33 teaches human monoclonal antibodies. Even assuming for the sake of argument that the disclosure is sufficient for the preparation of human monoclonal antibodies, one at best could only hope to obtain human monoclonal antibodies which specifically bind 499E9, and not antibodies which specifically bind human OPGbp.

Accordingly, human monoclonal antibodies which specifically bind to human OPGbp are not anticipated by the '586 patent. The rejection should be withdrawn.

Rejection of Claims 82, 83 and 85-92 under 35 U.S.C. 103(a)

Claims 82, 83 and 85-92 are rejected as being obvious over U.S. Patent No. 6,641,747 to Popoff et al. as evidenced by Yang et al. (Proc. Natl. Acad. Sci. USA 82, 7994-7998 (1985)) in view of Lonberg et al. (PCT Publication No. WO 93/12227). The Examiner notes that the claims recite a human monoclonal antibody that binds to an epitope comprising "at least part of" SEQ ID NO:39 of human OPGbp and alleges that the specification does not offer a definition of "at least part of". It is argued that the claims only require that the epitope of human OPGbp have at least one amino acid in common with SEQ ID NO:39 and, therefore, the antibodies that bind to and block the activity of activated vitamin D-binding factor (DBP-MAF) disclosed in the '747 bind to at least one amino acid common to both DBP-MAF and human OPGbp. The Examiner combines Lonberg with the '747 patent disclosure to argue that one would have been motivated to make human antibodies as disclosed in Lonberg for the purpose of developing a therapeutic antibody with desirable properties, such as reduced immunogenicity as compared to murine antibodies (the so-called HAMA response).

Applicant maintains that there is no specific motivation in the combination of the '747 patent and the Lonberg reference to make the claimed antibodies and therefore the Examiner has not established a *prima facie* case of obviousness. However, solely to advance prosecution and without acquiescing to the rejection, Applicant has amended Claims 82 and 85 to delete reference to "an epitope comprising at least part of" SEQ ID NO:39. In addition, Claim 86 has been amended to delete reference to an epitope "comprising at least part of" a BB' loop and Claim 87 has been amended to delete reference to an epitope "comprising at least part of" an EF loop. The rejection may be withdrawn.

Rejection of Claims 82-92 under obviousness type double patenting

Claims 82-92 are provisionally rejected under obviousness-type double patenting over Claims 2-9, 21 and 22 of co-pending U.S. application no. 10/180,648 (hereafter "the '648 application"). The Examiner argues that the claims of the '648 application are drawn to fully human monoclonal antibodies and compositions comprising antibodies wherein the antibodies have specifically defined heavy and light chain variable regions that inhibit the binding of human OPGbp to an osteoclast differentiation and activation receptor.

Applicant requests that further action on this rejection be deferred until such time as there has been an indication of allowable subject matter in the present application.

CONCLUSION

Claims 82-92 are in condition for allowance and an early notice thereof is solicited.

Respectfully submitted,

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